Exocrine Pancreatic Insufficiency after Gastrectomy for Cancer Is Not Severe

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Dear Editor,

I congratulate the authors of the Systematic Review of Exocrine Pancreatic Insufficiency (EPI) after Gastrectomy for Cancer [1]. The literature search identified 4 of 1,023 studies for review [2–5]. Overall, I agree with the authors' interpretation that EPI is common following total gastrectomy. Although the authors found that total exocrine pancreatic function decreases by as much as 76%, they do not sufficiently emphasize that the degree of EPI is typically mild to moderate severity following total gastrectomy with duodenal continuity, and specifically not severe enough to cause pancreatic steatorrhea, which requires a 90% reduction (of lowest normal values) in lipase output [6, 7]. Also, the authors did not include an older study investigating EPI following gastrectomy for cancer [8], which is worthy of consideration, particularly with the limited data available.

Critical points to interpreting the results of pancreatic function tests (PFTs) in post-gastrectomy patients are the use of accurate PFTs and the testing of patients with gastrointestinal continuity following gastrectomy. The most accurate PFTs were

used in 2 studies [2, 3] in the systematic review and in the additional study [8], each involving either secretagogue [2, 3] or test-meal [8] evoked direct PFT. All patients in the 3 studies had post-gastrectomy duodenal continuity of either jejunal interposition or esophagoduodenal anastomosis or jejunal pouch reconstruction.

In none of the 3 studies was EPI severe enough to cause steatorrhea, but it should be noted the sample size in each of the studies was very small, ranging 8–12 patients per study. Gullo et al. [2] performed secretin-cerulein stimulated direct PFT in normal controls and 12 patients following total gastrectomy with jejunal interposition or esophagoduodenostomy. Eight patients had gastric cancer. Gastrectomy patients had mild-moderate (38%) reductions in stimulated lipase output versus controls, insufficient to cause pancreatic steatorrhea [6]. Not surprisingly, lipase outputs did not correlate with steatorrhea (present in 8 of 12) [2]. Friess et al. [3] performed direct secretin-cerulein stimulated PFT in 9 patients with gastric cancer, both preoperatively and 3 months after total gastrectomy

with jejunal pouch. Following gastrectomy, median secretagogue-evoked juice values were reduced 72% for amylase (suggesting moderate EPI) and 89–91% for trypsin and chymotrypsin (suggesting borderline severe EPI). Importantly, the authors calculated the reduction of enzyme values from the median rather than the lowest normal or lower quadrant values resulting in greater calculated reduction of enzyme secretion than was present. Further, the authors did not measure lipase outputs. Thus the severity of EPI in the Friess study would be most consistent with mild-moderate EPI, which alone would not cause steatorrhea. Fischermann et al. [8] performed test-meal evoked PFT in normal controls and 8 gastric cancer patients who had total gastrectomy and jejunal interposition. The gastrectomy group had only mild-moderate reductions in test-meal evoked peak lipase concentrations.

The most plausible single explanation for mild-moderate EPI following total gastrectomy for gastric cancer is denervation (truncal vagotomy and interruption of gastropancreatic nerves secondary to lymph

node dissection). Reduced outputs in patients following gastrectomy (above studies) are similar to those in patients following truncal vagotomy, which causes reductions of lipase and trypsin outputs by 53 and 61% [9, 10]. Onset of steatorrhea following gastrectomy is most likely attributable to non-pancreatic causes, particularly post-surgical anatomy without duodenal continuity (e.g., Rou-en-Y), causing a mixing disorder (asynchrony between delivery of pancreatic enzymes and chyme) and maldigestion. Pancreatic enzyme replacement therapy (PERT) can correct the mixing disorder, but this does not equate to a diagnosis of EPI.

In 2 PERT trials [4, 5], a placebo-controlled RCT [4] and a cross-over trial [5], steatorrhea and lack of responsiveness to PERT are attributable to post-surgical anatomy, PERT dosing and non-pancreatic factors rather than EPI. Bragelmann et al. [4] reported PERT (76,000 FIP units of lipase per meal) did not reduce steatorrhea compared to placebo. Armbrecht et

al. [5] reported that PERT (120,000 units of lipase per meal) only reduced fecal fat excretion compared to placebo in the subset of patients with “massive” steatorrhea. These conflicting data are likely due to a higher frequency Rou-en-Y postsurgical anatomy in the Armbrecht vs Bragelmann studies (100 vs. 65%) but also due to under-dosing of PERT in the Bragelmann study (see review of PERT dosing [7]), exclusion of small intestinal bacterial overgrowth in the Armbrecht but not Bragelmann study, or other factors that may have caused steatorrhea in Bragelmann study [4].

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